

Capsid protein from WNV Cp also shares homology with capsid and other proteins of other viruses, including, but not limited to, viruses in the *Flaviviridae* family, and viruses from many other virus families. The WNV Cp protein also shares homology and with non-viral proteins, including proapoptotic proteins of mammalian origin. Regions of homology/identity have been identified between the WNV Cp and the HIV-1 Vpr protein (which has apoptosis activity), Cp protein from Kunjin virus, Cp protein from Japanese encephalitis virus, Cp protein from Dengue virus, major capsid protein from herpes simplex virus, Ebola virus nuclear protein, Ebola virus glycoprotein, Rubella virus capsid protein, and with the following proapoptotic, non-viral proteins: human BAK protein, human Bcl-2 associated X protein, human BIK protein, human BID protein, and human Bad protein. Moreover, regions of homology/identity have been identified between HIV-1 Vpr protein and the p230 nonstructural protein of Sindbis virus, the 2A protein of cucumber mosaic virus, Rubella virus capsid protein, Nipah virus fusion protein, reovirus core-minor form Mu2 protein, and with the following the proapoptotic proteins: mouse BIM protein, rat BOD protein, mouse Mtd protein, human Bcl-2 associated X protein, and human Bad protein.

One having ordinary skill in the art can readily determine whether a protein or peptide is a functional fragment of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein by examining its sequence and testing its ability to induce apoptosis in cells without undue experimentation. Truncated versions of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein may be prepared and tested using routine methods and readily available starting material. As used herein, the term “functional fragment” is also meant to refer to peptides, polypeptides, and amino acid sequences linked by non-peptide bonds, or proteins which comprise an amino acid sequence that is identical to, or substantially homologous to at least a portion of the WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein amino acid sequence, and which are capable of inducing apoptosis. The term “substantially homologous” refers to an amino acid sequence that has conservative substitutions. One having ordinary skill in the art can produce functional fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein following the disclosure provided herein and well known techniques. The functional fragments thus identified may be used and formulated in place of full length WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein without undue experimentation.

The present invention also relates to vaccines comprising immunogenic fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, and/or a nucleic acid encoding immunogenic fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, to induce prophylactic or therapeutic immune responses in individuals. As used herein, an “immunogenic fragment” of “capsid protein from WNV or a other viruses including *Flavivirus* or *Pestivirus*” refers to a fragment of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein which is capable of inducing an immune response. Immunogenic fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein are at least about 10 amino acids in length, derived from WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, and may comprise amino acid sequences that are not derived from WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein. One having ordinary skill in the art can readily determine whether a protein or peptide is an immunogenic fragment of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein by the use of classical immunological assays to screen for antibody production in response to immunizations with fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein. These include, for example, 1) enzyme-linked immunosorbent assay (ELISA), 2) proliferation assays of cells from lymphoid organs, and 3) evaluation of the number of cells producing antibodies to a given antigen. Detailed protocols for these standard assays can be found in such manuals on immunology as Weir & Blackwell, eds., Handbook of Experimental Immunology, *supra* and Coligan *et al.*, eds., Current Protocols in Immunology, *supra*. One having ordinary skill in the art can produce and identify immunogenic fragments of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein following the disclosure provided herein and well known techniques. The immunogenic fragments thus identified may be used and formulated in place of full length WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein without undue experimentation.

Therapeutic aspects of the invention include use of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, a functional fragment of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, nucleic acid molecules encoding WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or nucleic acid molecules encoding a functional fragment of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein in pharmaceutical compositions useful to treat an individual suffering from diseases characterized by or associated with hyperproliferating cells, such as cancer or psoriasis.

One aspect of the present invention is to use WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, or nucleic acid molecules encoding WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, in a pharmaceutical composition to combat diseases that are characterized by undesirable cells such as, but not limited to, those diseases characterized by the hyperproliferation of cells, such as cancer or psoriasis. According to the invention, pharmaceutical compositions are provided which comprise either WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, or a nucleic acid molecule which comprises a DNA or RNA sequence that encodes WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof.

Another aspect of the present invention relates to pharmaceutical compositions that comprise WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof; and/or a nucleic acid molecule encoding WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, and a pharmaceutically acceptable carrier or diluent. Pharmaceutical compositions comprising WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, and/or a nucleic acid molecule encoding WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, are useful for treating an individual having a pathology or condition characterized by hyperproliferating cells. As described herein, pharmaceutical compositions useful for treating diseases characterized by undesirable cells such as hyperproliferating cells may include WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, and/or a nucleic acid molecule encoding *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, since WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, are by definition, agents which induce apoptotic death in cells. Pharmaceutical compositions of the present invention are particularly useful for treating cancer characterized by solid tumors. The ability to stimulate hyperproliferating cells to undergo apoptotic death provides a means to disrupt the hyperproliferation of the cells, thereby decreasing the tumor. In diseases such as cancer and psoriasis which are characterized by the inappropriate hyperproliferation of cells, the pharmaceutical composition is useful to arrest the hyperproliferation through an induction of an apoptotic cell death, thereby effectuating a treatment of the disease.